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EXAMINER

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BEFORE THE BOARD OF PATENT APPEALS
AND INTERFERENCES

Paper No. 21

Date mailed 5/09/02

Application Number: 09/265,926
Filing Date: March 11, 1999
Appellant(s): DALES, JOHN ROBERT MANSFIELD

Thomas R. Savitsky
For Appellant

EXAMINER'S ANSWER

This is in response to the appeal brief filed 10/22/01.

(1) Real Party in Interest

A statement identifying the real party in interest is contained in the brief.

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(2) Related Appeals and Interferences

A statement identifying the related appeals and interferences which will directly affect or be directly affected by or have a bearing on the decision in the pending appeal is contained in the brief.

(3) Status of Claims

The statement of the status of the claims contained in the brief is correct. However, the rejection of claims 14 and 21 is dropped.

(4) Status of Amendments After Final

The appellant's statement of the status of amendments after final rejection contained in the brief is correct.

(5) Summary of Invention

The summary of invention contained in the brief is deficient because the examiner does not agree with the last sentence. Otherwise, the summary is proper.

(6) Issues

The appellant's statement of the issues in the brief is correct.

(7) Grouping of Claims

Appellant's brief includes a statement that claims 5, 6, 7, 10-14 and 21 do not stand or fall together and provides reasons as set forth in 37 CFR 1.192(c)(7) and (c)(8).

(8) Claims Appealed

The copy of the appealed claims contained in the Appendix to the brief is correct.

(9) Prior Art of Record

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(10) *Grounds of Rejection*

The following ground(s) of rejection are applicable to the appealed claims:

ANTICIPATION REJECTION

Claim 5 is rejected under 35 U.S.C. 102(b) as being anticipated by EP 302,644.

Claim 5 is drawn to a single species, depicted on page 6 of the specification, second species from the left in the first row. It is an intermediate for preparing BRL 42810. In the reference, note Formula I on page 2. This formula depicts a small genus of compounds of the same utility, intermediates for preparing BRL 42810. The claimed species corresponds to R_3 = amino, R_1 = methyl, R_2 = chloro.

There are clear preferences for all of these. R_3 has several choices, but amino is the most preferred, as it is the sole choice seen in the actual final product BRL 42810. As for R_1 , while several choices are listed, two choices are given as preferred at page 7, line 7, viz., methyl and ethyl. Further, claim 5 of the reference specifically names just the methyl and ethyl. All of the examples have either methyl or ethyl. For R_2 , there is a list on page 7, lines 8-9, which has 3 items in it, one of which is chloro (the other two are H and C_{1-4} alkoxy). Using these preferences, a Markush of $1 \times 2 \times 3 = 6$ members is obtained. Alternatively, the page 7, lines 8-9 list could be viewed as 6 items: H, Cl, and 4 alkoxys. Thus, by using the explicitly set forth preferred choices for these variables, a Markush $1 \times 2 \times 6 = 12$ members is present. A Markush group of such size is deemed to be an anticipation of all of its members. A genus this small is deemed to anticipate all of its members, *In re Sivaramakrishnan*, 213 USPQ 441 [genus of 70]; *In re Petering*, 133 USPQ 275 [genus of 20]; *In re Schaumann*, 197 USPQ 5 [genus of 14].

Appellants raise several rebuttals:

1. For R₁, "... although methyl and ethyl are the only specific moieties mentioned, they are not indicated as preferred..." This is a specious distinction. One of ordinary skill in the art would understand that when only two choices are specifically named, that is a clear blazemark that these are preferred.
2. For R₂, Appellants argue that the C₁₋₄ alkoxy should count not as 4 alkoxy groups, but as 8, covering the isomers such as sec-butyl. The examiner does not agree; isomers were not taken into account in *Petering*. However, even if this reasoning were accepted, that would give for R₂, 8 alkoxy plus H and Cl for 10, giving a genus of 20, enough for anticipation. Applicants also point to page 8, lines 29-30 where a broader definition of R₂ is given, and asks if this "should be ignored". This is a definition which is virtually identical to the main definition for R₂. It is not the preferred definition; that is given at page 7, lines 8-9.
3. For R₃, Appellants concede that amino is preferred for the final product BRL 42810, since amino is what BRL 42810 actually has, but does not see that as preferred for the intermediate, and points to broader definitions for R₃. It is agreed that there are other choices, but the fact that the final product has just amino surely makes amino preferred.
4. Appellants note that the examiner cites *Sivaramakrishnan*, *Petering*, and *In re Schaumann*, but that the examiner fails to cite either *In re Rushig*, 145 USPQ 275 or *In re Arkley*, 172 524. However, those latter two cases dealt with different fact situations.

In *Arkley*, the CCPA said, "In *Petering* we came to the conclusion that a specific compound ... was actually described in the Karrer reference patent by reason of the particular disclosure of that patent which we felt would be recognized by those of

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ordinary skill in the art as a description of some 20 compounds in a limited class, the members of which were very similar to one another in structure and all of which possessed the same properties.” That was not the case in *Arkley*, as was noted: “we do not find the present case to be of the type we had before us in *Petering* ... We would apparently get from the French patent some 130 and from the Swedish some 156 compounds.” The opposite is true here; the compounds the examiner refers to are all very similar in structure and are all of the same property. Appellants note that *Arkley* warns about “picking and choosing”, but the examiner does not do that here; the reference itself does the choosing by indicating what is preferred.

As for *Rushig*, there the CCPA felt that the Board was misreading the reference, saying that the Board “postulates certain teachings which might have been in the reference patent any one of which, according to it, if present would have removed all doubt concerning the completeness of the anticipation. The simple answer to the board's argument is that these teachings were not contained in the Flynn patent and that we do not regard the teachings which were there and which were relied upon below as the equivalent of those which were postulated by the board. We do not read into references things that are not there.” Such is not the case here. The examiner relies on specifically disclosed preferred language, and reads nothing into the reference.

OBVIOUSNESS REJECTION FOR CLAIM 5

Claims 5 is rejected under 35 U.S.C. 103(a) as being unpatentable over EP 302,644.

Insofar as claim 5 is concerned, note the above anticipation. Even if this is not small enough to establish a *Petering* type anticipation, a genus with at the very most a

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few hundred members is surely enough to establish obviousness. Note *Merck & Co. vs Biocraft*, 10 USPQ 2nd 1843, 1846, which had 1200, *In re Corkill*, 226 USPQ 1005, 1008 (a genus of thousands), *In re Susi*, 169 USPQ 423, 425. Here, not only is the genus which embraces the species much smaller, but there are, as set forth above, clear blazemarks to point to narrower choices for each of the variables. For example, in the claim, R₁ = methyl, and while there are several choices in the genus, all of the examples have either methyl or ethyl.

OBVIOUSNESS REJECTION FOR CLAIMS 6-7 AND 10-13

Claims 6-7 and 10-13 are rejected under 35 U.S.C. 103(a) as being unpatentable over EP 302,644. Note that the rejection of claims 14 and 21 is dropped.

The process of claims 6-7 and 10-13 and the prior art is virtually identical. Page 7 of the Appeal Brief sets forth the process of the working examples of the reference, and then the process of the instant case. These both start and both end with the same compounds. These both have the same coupling-decarboxylation-reduction-acetylation sequence. The sole difference between the process of the examples of the prior art, and the instant process, is that in the prior art, the 6-Cl is removed prior to decarboxylation, and in the present case, it is removed afterwards. If it were not for that single difference, the reference would literally be an anticipation.

However, the process as broadly described does not require that the Cl be removed prior to decarboxylation. The initial coupling in the first step gives VI (page 6, line 40). Then there is a decarboxylation, given at page 6, line 49, first word. The scheme does not require, indeed, does not even mention, removing the 6-Cl prior to this decarboxylation. The failure to mention removal of Cl between the two steps would

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indeed qualify as a teaching to one of ordinary skill in the art that the process can be done in exactly that way, can be done without an intervening Cl-removal step. Thus, the concept of coupling immediately followed by decarboxylation, which is what the claims have, is set forth in the overall scheme, even though the working example inserts the dechlorination at that point. Thus, applicants description of the reference solely in terms of coupling then dechlorination then decarboxylation simply ignores what is on page 6. Indeed, it is only later in the line (page 6, line 49), after the decarboxylation, that the option of changing other variables is mentioned (“interconverting” $R_2 = Cl$ to $R_2 = H$ or to OH is the removal of the 6-Cl step).

Appellants are correct that the preferred embodiment of the reference of the reference is a process in which the Cl is removed prior to decarboxylation. However, a reference is available for all that it teaches or renders obvious, not just the best or even the preferred embodiments. In this regard, see *In re Lamberti*, 192 USPQ 278, 280; *In re Boe*, 148 USPQ 507, 510; *In re Fracalossi*, 215 USPQ 569, 570. While it is unusual for the working examples not to follow the generic sequence, this does happen, as is present here.

The Brief states, “The process steps on pages 5 and 6 of the ‘644 reference do not teach when the starting material ... is to be dechlorinated.” That is true in the sense that removal-of-Cl isn’t specifically mentioned, only the broader “interconverting variables ... R_2 ... to further values ...”) However, even if broadly true, that just leaves when to remove the Cl open-ended. The fact that it is removed prior to decarboxylation in the examples would not act to preclude any other understanding of the process. This is especially true since the scheme literally states that one does coupling immediately

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followed by decarboxylation. Thus, even without any guidance, the scheme covers doing the (unmentioned) dechlorination at any time after decarboxylation.

The Brief at page 7 also makes mention of isolation steps. The reference does indeed have isolation steps along the way, a common procedure in multistep synthesis. The claims are silent on the subject of isolation steps or their lack, and lack of anticipation cannot be based on limitations not present in the claims. The claims use “comprises” language, so the claims are embrative of additional isolation and purification steps; there is no “one-pot” or “without isolation” language in the claims. Indeed, the actual examples of this specification do indeed involve isolation and purification; see e.g. last sentence of example 1, and last three sentences of example 2.

Having established obviousness, the burden shifts to Appellants to demonstrate unexpected effects. This should be straightforward. The prior art’s working examples are replicated, and applicants measure yield or purity or whatever variable they wish to use to demonstrate unexpected effects. This is then run a second time in the exact same manner, except that the Cl is removed earlier rather than later. This side-by-side comparison they have failed to do.

Appellants have presented a Jones declaration which failed to provide anything even close to a proper replication of the prior art process. In fact, declarant doesn’t even say that he replicated the prior art process. Instead, he calls it “EP 302644 Type process” (see e.g. first page of Annex). A large numbers of differences were introduced, differences which have nothing to do with claim requirements. The result of these differences was a failure to even obtain the prior art product! Specifically, the EP 302,644 reference starts where the declaration starts, and ends with the same

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diacetylated diol, yet applicants ended with a crude oil (called "useless" in the Appeal Brief, page 12) which they were unable to crystallize from n-butanol (page 6, step 2, item vii). By contrast, the EP 302,644 reference states that they were able to obtain colorless crystals from n-butanol, melting at 102 °C. It seems clear that these variations prevented a proper obtention of the results seen in EP 302,644. The changes they made ruined the process. The conclusion that the prior art process yields only a useless brown oil is directly contradicted by the fact that the EP 302,644 did in fact produce the compound as colorless crystals of the correct melting point. Thus, it cannot be argued that the differences were harmless; the differences, in effect, sabotaged the prior art process.

The Appeal Brief at page 12 , middle paragraph, is confused. It states that the contrast between EP 302644 giving a crystalline product "yet the process in our declaration gave a useless brown oil only further highlights the surprising advantages obtained using the process of the invention." But that specific contrast says nothing about the process of the invention. It only says that applicants failed to replicate the prior art results. Failures to properly replicate occur in three of the steps:

First, it does not properly replicate the prior art process for Stage 1, step 3, the decarboxylation of the triester. The change was so drastic that it actually results in a chemical process which is not recited in claim 10 or the reference. In EP 302,644, the process is set forth in Example 3, i.e. the conversion of starting material D12 (prepared in Description 12) to final product E3. This process appears as Step 3 on page 5 of the declaration, as is described on page 6, beginning on line 3. It is crucial to note that the starting material D12 is an ethyl ester. There are three significant differences:

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A. EP 302,644 uses NaOEt in ethanol; the declaration uses NaOMe in methanol. Thus, not only is a different reagent used by appellants for the decarboxylation itself, but a transesterification (ethyl to methyl) is also being done. Note that in the reference, the conversion of D12 to E3 is not a transesterification, as one goes from the ethyl ester D12 to the ethyl ester E3. But in the so-called replication, the ethyl ester is transesterified to the methyl ester. See Declaration, page 4, last step of the scheme. Note that the Et becomes Me in that step! Further, note that the rejected claims do not require a transesterification either and indeed make no mention of transesterification, as they simply call the process a decarboxylation. Thus, a proper comparison in the declaration would have used NaOEt in ethanol in both the EP 302,644 and the claimed process. Neither the declarants nor the Appeal briefs make any explanation of why a transesterification step was slipped in, when neither the reference nor claim 10 makes any mention of such a step.

Appellants in the last full paragraph of page 12 of the Appeal Brief address this issue. They make no attempt show that the prior art process ever contemplated a transesterification. Instead, they rely on the "comprises" language to argue that the it literally falls within the claim, even though it is not set forth. However, the prior art process does not have transesterification, and the claims do not even mention it, so the comparison should have been done on the basis of an overall process which did not involve transesterification.

B. EP 302,644 acidifies the mixture to pH 3 prior to solvent evaporation. The declaration process has no such step. No explanation appears as to why the prior art acidification step was omitted in the replication.

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C. EP 302,644 purified the material, including a drying process, which converted the yellow oil to a crystalline solid. No such process occurs in the declaration. No explanation appears as to why the prior art drying step was omitted.

Second, the reduction to diol (stage 2, step 1, at page 5 of the Jones declaration) in the EP 302,644 process was done differently from what appears in the actual reference on page 18, step a). (The examiner assumes that the "6-Chloro" at the sixth from last line of page 5 of the declaration is a typographical error).

D. In EP 302,644, the reduction is done in t-butanol; in the declaration, in dichloromethane. One is a protic solvent, the other is not.

E. In EP 302,644, the reduction is done at reflux; in the declaration it is done at 20 °C. This is a very substantial difference in temperature, and temperature is generally understood by the synthetic chemist to be a variable which can readily affect results.

F. In EP 302,644, the methanol addition was done without chilling; in the declaration, the reaction mixture was chilled to keep it at room temperature.

G. In EP 302,644, the product is purified by chromatography before the acetylation; this step does not occur in the declaration. This is potentially important because the product is described in EP 302,644 as being a white solid, whereas in the declaration it is described as being yellow colored (declaration page 6, line 8). This means that it is likely that the EP 302,644 process produced a purer product than the declaration process, vitiating the comparison.

No explanation was given as to why the declarants skipped the purification process taught by the prior art, or why changes were made in solvent and temperature.

Third, the acetylation of the diol (stage 2, step 2, page 6 of declaration) in the process was done differently than what actually appears in EP 302,644 on page 19, step c):

H. In EP 302,644, there was used THF as solvent along with pyridine. In the declaration, there was used dichloromethane as solvent plus triethylamine. THF is a much more polar solvent.

I. The workup was completely different. For example, in EP 302,644 there was a drying process and column chromatography; neither was seen in the declaration, which used an extraction process.

No explanation appears as to why these two differences were introduced.

Attached also to the Appeal Brief is a Geen Declaration of 15 December 1999. This does not provide anything additional, and has essentially the same problems.

Appellants disagree with the examiner's statement that they "must compare to the prior art process.", stating that "this is an inaccurate statement" (Appeal Brief, page 11).

It is well established that a declaration under 37 CFR 1.132 must compare the claimed subject matter with the closest prior art, to be effective to rebut a prima facie case of obviousness. See *In re Burckel*, 592 F.2d 1175, 201 USPQ 67 (CCPA 1979) and *In re Merchant*, 575 F.2d 865, 868, 197 USPQ 785, 787 (CCPA 1978). Note in particular *In re Armstrong*, 280 F.2d 132, 126 USPQ 281 (CCPA 1960) where the deviations from the example were considered inconsequential. Such could not possibly be the case here, since the deviations are so numerous and so substantial.

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Applicants instead point to *In re Yan*, 175 USPA 96, which says, “it is not mandatory in every case to compare a claimed process with a prior art process in their entireties in order to establish the patentability of the claimed process.” The key phrase in that quote is “in their entireties”. In that case, Applicants needed to establish just a specific fact, and the decision goes on to state on page 99 “We agree that the full processes need not be run to establish this factually...” There is nothing in that case to support the notion that applicants can make wholesale revisions in a prior art process, but rather that applicants did not have to run the entire process just to establish a fact that concerned just one aspect of the process.

Appellants have introduced a total of 9 significant changes in three different steps of the prior art process, resulting in a failure to even obtain the product that the prior art reports. Hence, they do not have a proper comparison with the prior art and have not overcome the obviousness.

For the above reasons, it is believed that the rejections should be sustained.

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Respectfully submitted,



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Primary Examiner
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January 24, 2002

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